# AMERICAN JOURNAL of PHARMACY

SINCE 1825

A Becard of the Progress of Pharmacy and the Allied Sciences

COMMITT	TOTAL C	180	DITE	LICA	TION	ĕ
	1 1 2 1 2 1	7 X 10	1 64 7 7 1 7	10 J. 10 T.	di di Calif	a

Charles H. LaWall, Ph. M., Sc. D. John K. Thum, Ph. M.

Arno Vichoover, Ph. D. IVOR GRIFFITH, Ph. M., Editor

Henry Leffmann, A. M., M. D., Special Contribute

Vol. 99

JANUARY, 1927

No. 1

## CONTENTS

Editorsa:			
	B GEORGI	140 000	C 248
		Acceptance	

The	New	Year	Hill
The	Metri	c Di	spute

# Selected Editorial:

# The Scientist and the Alcohol Question ......

Sophistry.	By	john	Uri Lloyd,	Cincinnati,	Ohio
		Section 1	SHOW IN COLUMN		1000

	deliber.	<b>School</b>	Na Pine	delication delication de		CHICKING	A CONTRACTOR
Calcium	Salts	of I	wo	Tempera	ture	Tar	Phenols

		THE RESERVE AND ADDRESS.	200			
Our	Science	Exhibit.	By	Arno	Viehoever,	Philadelphia

Prof De	Alexander	Tschirch-A	Tribute	R. F	Fullecton	z
C -it-	1 FICKERGET	A SCHILL CH-12	THOME		T. HIVEL COST	2

EDEDING.	lei fisione e e e e e e e e e e e e e e e e e e	DOM: N	A CONTRACTOR	Section 2		100000		65) Sec. 30	MA 10 23	BOARS I
Dr. G	eorge	D.R	osengarti	en Ba	1 1	N Eng	dond	Philade	lohia	

Note on the Diethylphthalate Test.	Reprinted from	Journal	Assoc.	of Offic.
Agric. Chemists				

Aniline Dyes in					
and Engin.	Chemis	try	 	 	***********

Tabloid	Tales of	the P	rogress of	Science	in 1926		A	36

Medical and Pharmaceutical Notes	12	
	200	

News Items and	Personal	Notes	
Book Reviews			

Price \$3.00 per Annum in Advance

Poreign Postage, 25 Cents Extra

By Frederick R. Green-

ook, Bern

Single Numbers, 30 Cents. Back Numbers, 50 Cents

Entered as Second-Class Matter at the Post Office at Philadelphia, Pa., Under the

Acceptance for Mailing at Special Rate of Postage Provided for in Section 1908, Act of October 3, 1917. Authorized February 15, 1920

PUBLISHED MONTHLY BY THE

Philadelphia College of Pharmacy and Science

145 North Tenth Street, Philadelphia

# American Journal of Pharmacy

#### ESTABLISHED IN 1825

Four preliminary numbers were published at different times until in 1829, when the publication of the regular volumes began. Since then the publication has been uninterrupted. During the period from 1829 to 1852 four numbers were published annually, except in 1847, when five numbers were published. From 1853 to 1870 six numbers were published. Since this time twelve numbers have been published annually.

MANUSCRIPTS should be sent to the Editor. It should be stated in this connection that the Editor does not assume any responsibility in connection with the views or investigations of contributors, other than to exercise general care in the selection of matter.

Contributors are allowed a reasonable number of copies of this Jour-NAL, free of charge, if applied for when the proof is returned.

REPRINTS, if desired, must be applied for when the proof is returned. The table belows shows the approximate cost of reprints, the males-up of the pages to be identically the same as in the JOURNAL. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, etc. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

		s pp.	4 pp. 8 pp.		16 pp. C		OVERS WITH TITLES	
25	copies	\$2.25	\$3.75	\$7.75	\$9.00	25	copies	\$1.75
			4.00	8.25	9.75	50	4	2.00
100		2.75	4.25	9.00	10.75	100	•	2.25
250	•	3.75	4.75	10.00	12.00	250	*****	2.75

Our readers will find it to their advantage to carefully consult the advertising pages when desiring to correspond with STRICTLY PIRST-CLASS PARTIES.

Chens. Ris Pharms. Walus

# THE AMERICAN JOURNAL OF PHARMACY

Vol. 99

JANUARY, 1927

No. I

# **EDITORIAL**

#### THE NEW YEAR

A S THE pencil moves to write this little salutation the mind lags by a bit and stubbornly notes that only a flickering wisp of time has spent itself since last we penned such greetings.

Yet into this microscopic mite the fates compressed a deal of action—much that was glorious and some that was not—sorrows that came to some and the joys that thrilled others. There were great accomplishments and greater disappointments. Truly enough the holy hymn sounded on holidays, but jazz filled the rest of the calendar.

Science in its forward march has emulsified religion and the creed of Corinth has been made to suffer at the hand of crude technicians, of whom faith is no part. Such was the story of 1926.

But it is to the New Year that we now pay homage. Clean and new, like the calendar that stands on our desk, it comes brimful of promises and pulsing with possibilities. With hope we salute it.

Better than we could even hope to write, another has written a ringing message. It formulates a creed and expresses a wish, sublime enough yet practical enough for everyone to utter—and to hope for. It is this:

"The sun is just rising on the morning of another day, the first day of a new year. What can I wish that this day, this year, may bring to me? Nothing that shall make the world or others poorer, nothing at the expense of other men; but just those few things which in their coming do not stop with me, but touch me rather, as they pass and gather strength: A few friends who understand me, and yet remain my friends. A work to do which has real value without which the world would feel the poorer. A return for such work small enough not to tax unduly anyone who pays. A mind unafraid to travel, even though the trail be not blazed. An understanding heart. A sight of the eternal hills and unresting sea, and of something beautiful the hand of man

M. F. M.

has made. A sense of humor and the power to laugh. A little leisure with nothing to do. A few moments of quiet, silent meditation. The sense of the presence of God. And the patience to wait for the coming of these things, with the wisdom to know them when they come."—W. R. Hunt.

We can wish for our readers no saner, no kinder, no worthier wishes than are expressed in the quotation above.

Let us be thankful as we hurry on, that time, the immutable, suffers us to wish and to remember, to fashion dreams and fill our hearts with memories.

IVOR GRIFFITH.

#### THE METRIC DISPUTE

"The war, which for a space did fail, Now, trebly thundering, swelled the gale,"

EVERY NOW and then an active propaganda develops for extension of the use of the metric system among English-speaking people, and is met promptly by counterblasts. As with all such issues, the opposition consists of groups with different principles. A limited number of well informed and experienced workers consider the system of little advantage and believe that the one in use can by simple modification be made to serve perfectly. With very many the attitude is indifference, but a large proportion of this group can be rallied to the opposition, if aroused by some talk as to the possible inconveniences or confusion that a change will cause. The mass of the community does not understand nor care for the philosophy and science of units and standards. The principal business of happy countries, such as the British dominions and the United States is housekeeping. The housewife desires no change in units. She buys sugar, butter and meat by the pound, eggs by the dozen, fruits by the peck, textiles by the yard, fuel by the ton, soap by the cake and the table accessories by the can. It is not likely that the adoption of any new system of weights and measures would make much change in market methods. In fact, in shipping circles there is largely used a sort of mongrel unit the "metric ton." It is 1000 kilos and therefore is closely equivalent to the standard "long ton" of British and American use.

Of course, opposition to the metric system is in many cases merely temperamental—opposition to change. It is akin to the opposition to phonetic reform in English spelling by those who do not want to see the "glorious language of Shakespeare and Milton" abandoned. Many of these are unfamiliar with the original texts of these authors, and do not know, for instance, that Shakespeare spells "politic" and "music" with a final "k." The reform of the calendar established by Gregory XIII, was resisted by English-speaking nations for over one hundred and fifty years, being adopted by Act of Parliament in 1752, by omitting eleven days in September, calling the day following the second of that month the fourteenth. It is said that a mob filled the streets of London shouting "Give us back our eleven days."

In a recent number of this Journal, Mr. Wilfred Lewis makes a strong appeal against the adoption of the metric system. He is a mechanical engineer of high training and large experience and his views must be received with respect and attention. He has been for years active in opposition to the adoption of the system. An examination of his statements in the article shows that he deals practically with the units of length. Volume and weight are but little considered. If the question was only with linear measures there would be no great concern. The mile is as convenient as the kilometer, the foot as the meter and the inch as the centimeter, especially if the practice of dividing the last-named decimally should become general. It is with gallons, pounds, ounces and their subdivisions and multiples that the difficulty arises. There are two pounds, each having its ounce, and to make matters worse, the troy ounce is heavier than the avoirdupois but the latter pound is heavier than the former. There are two gallons, ale and wine (pace Volstead) and each has its pints and quarts. Then there is the fluid-ounce different from the other two.

There is no convenient inter-relation between the weights and measures of the British-American system. The metric system gives us very convenient relations between these, so that solutions of given strength can be made up quickly and without much liability to error. An advantage of the metric system is that the units are international. By the adoption of them a large amount of confusion and uncertainty will be avoided. In the present tendency to close intermingling of the nations, uniform systems of all kinds are useful. Many persons are striving to secure the adoption of a universal language. In the

interest of international unity, the countries of the Greek church have recently accepted the Gregorian calendar, doubtless amid the tears of many of the ignorant and some of the learned.

Scientific workers, especially in chemistry and physics, have long since recognized the value and convenience of the metric system. Perhaps the benefit derived has made them over-enthusiastic as to its merits and neglectful of some defects. They have been "to its faults a little blind and to its virtues very kind." Like all systems of human origin it is not perfect. It was intended to be an absolute unit, the original datum being capable of re-ascertainment, but it is now known to be merely arbitrary. This is no argument against it for all other standards of its class are equally arbitrary. One minor difficulty about it is the multiplicity of divisions. Kilometer, meter and centimeter would be enough for measures of length; kilogram, gram and centigram for weight, and liter and cubic centimeter for volume.

It would be a sad day for research scientists to be deprived of the use of the system. This may seem impossible, but when we remember what has lately occurred in the restriction of education in certain departments of natural history under the pressure of a large class of ignorant persons, led by certain intellectuals, we may have some fear that the well-informed and well-meaning, but somewhat highstrung opponents of the metric system may get legislation against it. In fact, some movements in this direction have already been made.

HENRY LEFFMANN.

# SELECTED EDITORIAL

# THE SCIENTIST AND THE ALCOHOL QUESTION

By Dr. H. E. Howe

Editor, Industrial and Engineering Chemistry

PROFESSIONALLY the scientist is interested in but two sorts of alcohol. He requires the purest of alcohol, whether it be methanol, ethyl or grain alcohol, or one of the so-called higher alcohols for his research work. This in educational institutions can be obtained tax-free in accordance with established regulations. If he is connected with the industries, he recognizes that alcohol is second only to

water in its importance as a solvent and he requires large quantities at a low price for manufacturing purposes. Twenty years ago laws were passed to encourage industry by providing for denatured alcohol which could be sold tax-free, after having been rendered unfit for drinking by the addition of methanol or wood alcohol, pyridine, benzol, and a large number of other substances. These substances were chosen with a view to rendering the alcohol unfit for drinking without interfering with the industrial applications intended, and many chemists co-operated in devising the formulas which at one time or another have been approved by the Treasury Department.

The layman has little appreciation of the wide use of industrial alcohol and the fact that many materials cannot be made without it. Literally hundreds of thousands of dollars have been spent in an effort to find satisfactory substitutes for alcohol in the industry, since obviously no manufacturer would submit to present-day regulations on a basic raw material if he could use something else.

The practice followed by the federal authorities in denaturing alcohol is not materially different from that approved by many other countries; and indeed methanol, against which attacks have been launched in the past several months, is used in much larger quantities abroad than in alcohol denatured under the regulations of the United States Government. The industries have no objection to methanol and complaint comes either from those who desire to unravel denatured alcohol in order to divert it into beverage channels, or from the group who are opposed to prohibition and who have apparently decided to harass all and sundry to the point where they fancy some united demand may be made for the repeal of prohibition. Whatever the individual views may be concerning prohibition, industrial chemists are united in opposition to the tactics being employed, which if continued in the press and by politicians may lead to a situation where industry will find it necessary to fight for a raw material that has become essential.

Care is taken to market completely denatured alcohol under poison labels. The material as it leaves the hands of the denaturer is not potable, and yet those who would criminally manipulate this material seek to charge the Government with death which may occur from the illegitimate manipulation and use of this chemical compound. Industry finds it necessary to continue under existing conditions, while at the same time seeking the ideal denaturant which thus far no one has dis-

covered. The alcohol producers have established a fellowship at Mellon Institute and have taken other steps to co-operate in this search.

If those who are so largely protesting the use of methanol do so in good faith, an equal amount of energy contributed to the efforts to find an ideal denaturant would be far more constructive and much more in line with the interests of the industry as well as of the people at large.—(Science Service.)

# ORIGINAL ARTICLES

### SOPHISTRY\*

John Uri Lloyd, Cincinnati, Ohio

NOT VERY far do we have to travel to find people whose ideals are perhaps one-sided, in that what they do not desire, their neighbor must not have. Very willing are they to help make restrictive laws applying to the other man. In this sense, some academic pharmacists or psuedo-pharmacists are prone to go even further than the regimen of long established written laws, and demand that what the other man has acquired must, without recompense, be shared with himself. Let us consider the problem with a backward glance.

One might imagine that the speaker has in mind a material something that can be weighed or measured, and thus divided and subdivided. Such is not the case. Indeed, the material, in his opinion, is but an incident to imponderable mind, spirit, life. Unreachable force, such as energy expressions, light, heat, electrical phenom-"Imponderable" bodies one and all, generally lie far outside and beyond the scope of him who by rule of thumb deals in weights and measures. In their spheres of activity, matter becomes and is a plaything. But not of things afar off, or those in distance immense, do I speak today. The mote in our eye concerns us more than does a burning world near a distant sun, or an elephant in a tropic jungle. To the lad in school, self is apt to appear more important than all creation outside. We of this society, be we young or blessed with failing eye and wobbling feet of age, may well cast self aside, and turn thought to problems that confront the struggling youth coming into the field we yet occupy, but must soon relinquish.

<sup>\*</sup>Fragment from a former lecture, date unknown, as well as society where delivered. J. U. L.

Sophistry.—Is not the person, be he a man of wealth or an educator, who asks a lad to spend his parent's savings and devote years of his life to the gaining of an education applicable to pharmacy or medicine, and then denies him the privilege of legitimately applying the result to his own life's advantage under protection of our country's laws, illogically and thoughtlessly practicing sophistry in a most pronounced form? Can a boy become a theoretical idealist to the extreme, and yet partake of life's opportunities as do others not thus weighted? Can he succeed as he should in the world of business. where he is confronted by minds fully as bright as his own, and whose thought is of money alone, reinforced, perhaps, with inherited loads of money? Do not such as these monopolize every field, as giants? Are they not his competitors? Can the idealistic ethics of a person concerned in pure science, with salary secure for life, to whom business problems are remote, be applied with justice to an emptypursed boy, struggling not to be a teacher or a discoverer for others' good, but merely for a place in business, bettered by his education? Is it desirable thus to embarrass him in his attempts?

Have not years of that young man's life been sacrificed in attaining a well-earned educational advantage over others who have made no such sacrifice of time and money? Has that boy gained his imponderable (mental) equipment vainly, in the hope that by its utilization the very necessities, perhaps, of life may be better attained than is possible to one who has never sacrificed as he has, through years of study and research?

Laudable is the cry of him who, needing no money, advocates the application of higher academic ethics to the very limit, for those alone concerned in his own restricted sphere. But life, to most of us is real, not theoretical, nor yet hypothetical. Should not each youth who goes into the world without the inheritance of a load of gold, be encouraged to plan, experiment, discover by research, and balance conditions from his own point of view, be this ambition only for materialistic self-profit? Must he who has only brain wealth, seeking to utilize this as honorably earned business knowledge, not be encouraged to use this knowledge to help his fight for position, under the laws of the land, be he where he may? Is the son or heir of the man of wealth who can employ the man of brains, to become a standard for us all?

As I now look at the problem, and as I have ever viewed it, the gaining of an education, be it by empirical practice or by systematic

8

iı

n

ti

aı

le:

an

schooling, be it in broad lines or as applied to a specialty, is, as a rule, to serve the recipient's interest. First, in the enjoyment that comes from intellectual superiority, and next, service to others, as well as business returns to himself. Are not such objects, like, honorable and dignified?

Few of the thousands who graduate in pharmacy or medicine, expect to become professional teachers or purely academic professional men. The majority must apply themselves, often unrestrictedly, to what is called "business." Only the ultra-theorist, willing and able to be a hermit (usually because of the help of relations or others), afar from life's cares, will exclude the term "business" from his professional career. And often the business of the "hermit," himself, is a selfish ambition to be considered "queer."

The teacher's position is a noble one. His it is to inspire and instruct his classes. For this he is remunerated. The business man's duty is to supply materials needed by the public. From this comes as a return, a not less honorable emolument.

Let us cut business ambition out of American life, if the destruction of America be one's object. Let us suppress the educator, if America's foundation-stone is to be shattered. Twins are they, in civilization's progress!

In the last analysis, one might ask, Is business degrading, as contrasted with professional service? Can true professional men separate themselves, "intellectually," from those in business? Is it possible to discriminate concerning the relative importance of "think," in connection with the two classes of humanity? Pure ethics may become a mighty poor food provider, if such a thing as "pure ethics" exists.

Consider, as an ethical standard, the very highest ideal in our phere of pharmaceutical and medical instruction—the University professor, qualified to the limit in schooling. Is he not also concerned in business? Business embraces finance, resting on money. Does not this professor take money for his services? Precious few educators support their families on inheritances from their forebears, or on gifts from relatives. And of those who do, one might ask, did not their supporters obtain their money in some kind of business, or from investments dependent on business? May it not sometimes have been very questionable business?

1

r

đ

r

Imagine a questioner who may argue that an endowed institution stands above and beyond money cares or needs. Grant this, if such an institution exists, and we may ask how *the donor* who made that institution possible, got his surplus wealth? Dangerous is it to be too inquisitive.

Take now the successful pharmacist who utilizes his knowledge apparently in business processes only. Is he not also a teacher? Does he not, by his very success, show others in his calling how to succeed? Is he not a great inspiring object lesson? Is he not a prey to the imitator? If he makes a failure, does not that failure give others a lesson? Are not failures, in their end reactions, often of greater educational and economic value than successes? Let us ask, Is the business man, alone, subject to money failure? Are there no educational institutions that run behind in their finances?

Apply this thought to the teacher who, seemingly, is not in business. Are there no intellectual failures in his field? Are all alike successful? Does not one man succeed as a teacher, where others fail? Is not this success due often (perhaps always), to the fact that the man who succeeds applies "business think," business methods, to further his opportunities in his loved profession?

Sum it all up. Think further in this line. Who pays the taxes that support the public school, the college and the university? Who makes donations thereto? How is this money obtained? Do we look that gift horse in the mouth?

Is it less proper for a man in business to aim to excel in business, as an object lesson, than for him who teaches as a professional business, to aim to place himself in the very front rank of his profession? Has the business man no right to any ambition beyond the dollar?

Is it not a privilege for him to work, to accumulate, and finally, (or in the passing along), to comprehend the necessity of distributing a part, or even all, in the education or service of others? Is it not perhaps his greatest pleasure to utilize, in the interest of others, a part of such acquisitions as have come to him? Cut his contributions and donations from religion, from education, from exploration and from sanitation, if one dare attempt it.

Back we come to the heading that has led to these thoughts.

If a teacher or manipulator of ethics in pharmacy or medicine, leads a lad to spend his time and money to gain a scholastic education, and then, by an artificial course of reasoning that does not apply to life as others live, denies that lad the privilege of utilizing his knowledge according to his country's legal methods, the word "Sophist" may apply very kindly to that teacher. He covers the shortcomings of the past, and hides the necessities of the present and future from himself.

# CALCIUM SALTS OF LOW TEMPERATURE TAR PHENOLS

By Frederick R. Greenbaum, D.Sc., Philadelphia, Pa.

THE HIGH toxicity of low temperature tar phenols suggested the preparation of their calcium salts for use as an insecticide. These calcium phenolates might be successful in combatting the boll weevil, an insect which causes great damage to the cotton fields. At the present time, calcium arsenate is used; but its price is rather high and a cheaper substitute would be very desirable.

The preparation of the calcium salts of low temperature tar phenols offered more difficulties than were anticipated. The first experiments were based upon the double reaction between sodium phenolates obtained by the extraction of low temperature tar with sodium hydroxide and milk of lime, according to the following equation:

 $2C_6H_5ONa + Ca(OH)_2 \rightleftharpoons C_6H_5O - CaOCH_5 + 2NaOH$ 

This is apparently an equilibrium reaction taking place from the left to the right of the equation, particularly with high boiling phenols which form insoluble calcium salts. It was therefore necessary to find another method of preparation.

It is well known that if carbolic acid is heated with milk of lime under stirring, and is then filtered, the filtrate evaporates and leaves a calcium carbolate which is water soluble. The homologs of the phenol, however (such as cresols, xylenols, etc.), when combined with milk of lime, form insoluble calcium salts. This method was now used on low temperature tar phenols. Low temperature tar phenols or fractions thereof were heated with milk of lime under continuous stirring for several hours. When this was filtered the precipitate contained the formed calcium phenolates mixed with calcium hydroxide.

n.

1-

199

111

d

ie

er

IT

st

n

g

f

d

f

đ

S

r

r

e

The content of calcium phenolates in this mixture was determined in the following way: A weighed amount of the brown dried powder was covered with water in a beaker, and hydrochloride (1:1) was added and gently heated. The hydrochloric acid liberated the phenols from the calcium phenolates and dissolved the calcium hydroxide to calcium chloride. It was found that when it was heated for one hour on a water bath under frequent stirring, the liberated phenols floated upon the liquid. This liquid was poured into a Babcock bottle and the quantity of phenols could be measured directly in the narrow graduated neck of the Babcock bottle. From the amount of phenols, the amount of calcium phenolates could be calculated.

The values thus obtained were always very low and the content of calcium phenolates therefore rather small. This shows that the reaction between phenols and milk of lime is slow. If calcium chloride is used instead of calcium hydroxide, no reaction occurs; but if calcium chloride is used together with calcium hydroxide, the yields are essentially increased. The yield was found to be much better in aqueous than in alcoholic solution; it was also found that an excess of milk of lime is very effective in inducing a greater amount of the phenols to react with the calcium hydroxide, and that the reaction lasts from six to twelve hours. The presence of an organic solvent, such as alcohol or benzene, is detrimental and causes a decrease in the formation of calcium phenolates.

Yields of about 55 per cent. of calcium phenolates could be obtained by the following method: 450 g. of distilled low temperature tar phenols were mixed with 170 g. of calcium chloride and 115 g. of calcium hydroxide, in 300 cc. of water in a flask. This mixture was heated with a reflux condenser under continuous stirring for six It was then filtered, and washed first with water and then with benzene, to dissolve the free phenols which did not enter into reaction. About two liters of benzene were necessary to extract all of the free low temperature tar phenols. The precipitate weighed 269 g. and represented a mixture of calcium phenolates with lime. The wash benzene was distilled and produced 211 g. of phenols; so that 239 of the 450 g. of phenols used entered into reaction (a little over 50 per cent.). The analysis of the so obtained calcium phenolates gave 55 per cent. of calcium phenolates and 45 per cent. of calcium hyroxide. The unchanged and recovered phenols were again treated with a mixture of calcium chloride and milk of lime, and again yielded 165 g. of a mixture of calcium hydroxide and calcium phenolate, although there were only 30 per cent. of the latter to 70 per cent. of the former.

The mixture of 55 per cent. of calcium phenolates of low temperature tar phenols was sent to the boll weevil research laboratories in Tallulah, La., to be tested for its activity towards the boll weevil. The calcium phenolates, however, were found absolutely inactive against the boll weevil. This, however, does not exclude the possibility of using the calcium phenolates as an insecticide for other insects.

#### OUR SCIENCE EXHIBIT

#### Dr. Arno Viehoever\*

YEARLY the scientists of the country, joined together in the American Association for the Advancement of Science, come together for a week following the Christmas holidays; they exchange views, look for the encouragement which comes from the contact with the work and methods of others, and acquaint themselves with new tools, developed to increase the efficiency of scientific and educational work.

For the first time Pharmacy, having been recently affiliated with the organization, was included in the group. The meeting was held in Philadelphia—the historical center of Pharmacy. It occurred to the writer to prepare an exhibit broad enough in scope to be of interest to educators and scientists in the various lines of natural and medical science.

The following five phases of work were exhibited.

#### I. Creative Education

Individual student models of biological plant structures,—mechanical, where possible,—were shown as a new, effective method of teaching. Fig. 1. The home work of Freshman students represented models of

<sup>\*</sup>Director of the Biological and Micro-analytical Laboratories and Experimental Gardens of the Philadelphia College of Pharmacy and Science.

- (1) Cellsap-conducting tissue: Trachea
- (2) Insulating (heat and moisture) Tissue: Cork
- (3) Breathing Tissue: Stomata
- (4) Mechanical Tissue

Bone-like, strong—Sclerenchyma cell Muscle like, strong—flexible: Sclerenchyma fiber.

The making of individual models, worked out of any suitable materials, presents a severe test on the student's detailed knowl-



FIG. 1.—SCIENCE EXHIBIT.

Left: Plant Research: Digitalis (Heart tonic)—Beans of the Lima type; (Phaseolus lunatus); (Simaba Cedron, Central American febrifuge). Right: Creative Education: Biological Structures—Student models.

edge and resourcefulness. It trains his powers of observation and reasoning. It appeals to his desire to compete and triumph.

# II. Improved Tools and Apparatus

New apparatus were shown, partly made or suggested by students to assist in the work on micro-analysis. Fig. 2.

A micro-burner by Mr. Wilkins, extractors by Mr. Geiter and Mr. Deuble, micro boiling point apparatus by Dr. Shinohara, glass knife, utility knife with exchangeable blades for micro sections, sublimation and sedimentation apparatus by Dr. Viehoever and micro melting point apparatus by Viehoever and Clevenger.

# III. Plant Research and Biological Engineering

(1) Plants and seeds were shown of six Digitalis species—e. g., Purpurea, Lanata, Ambigua, Lutea, Siberica and Peruginea as well as substances isolated from the seeds of the official species D. Purpurea, e. g., drying oil, digitonin and digitalein. The characteristic vein distribution in the leaf was enlarged and illuminated by means of a new apparatus. Photos of plants during various stages of growth—including regeneration from leaves and (2) many microphotographs of the active substances and their hydrolysis products from both the seeds and leaves were exhibited.



FIG. 2.—SCIENCE EXHIBIT.

From Left to Right: Micro-analysis—Beans—Digitalis, Cedron, Models, Photographs and Microphotographs of Digitalis and Beans, and Glands. In Lower Center: Photograph of Lloyd Apparatus and Publications.

- (2) Seeds of Simaba Cedron, the intensely bitter glucoside "cedrin," fatty oil and wax, isolated from this Central American febrifuge, were shown in addition to photographs of the seed, fruit and tree.
- (3) Many varieties of Beans of the Lima type (Phaseolus lunatus) showing the wide range in yield of hydrocyanic acid were exhibited as well as the bitter hydrocyanic acid glucoside "linamarin." The beans were classed as: Harmless Beans—"Limas" grown in the United States, Doubtful beans grown in South America and Harmful beans—grown in Central America, India, the Philippines and

Java. The amount of hydrocyanic acid in the many varieties may vary from traces to over 0.3 per cent. A simple test, the exposure to ammonia was demonstrated; it colors certain portions of the beans of the lima type bean yellow—e. g., the hilum, where the seed is attached to the seed pod. No beans belonging to other Phaseolus species have been found to give the test as was demonstrated with Navy, Kidney and Spanish beans. Photos and micro-photographs bringing out the morphological and anatomical structures of Phaseolus Lunatus and other Phaseolus species (plants and seeds) were displayed.

#### IV. Glands and Glandular Products

Various glands: Pancreas, Thyroid, Corpus luteum, the Ovary, Pineal and Pituitary were shown, as well as the distribution of glands in man. A photograph illustrating our J. Uri Lloyd extraction apparatus, suitable for extraction of plants and animal products, was also exhibited.

### V. Recent Scientific Publications

Both technical and popular. Copies of articles on "Experimental Gardens"—were placed near the Exhibit and it was very gratifying to realize the extensive interest in this pamphlet—over 250 copies were taken. Recent theses and articles by the writer on Imitation of Life, Control of Growth—Biological Engineering, Cotton Glands, etc., as well as copies of *Popular Lectures* were displayed and attracted much attention.

The personal comments made by the many interested educators, scientists and other visitors were very encouraging indeed.

In the Summary of the Science Exhibition—published in the Supplement No. 1 to the General Program—we find the statement, "A most interesting exhibit of models of biological structures made by students together with photographs and research items."

#### PROF. DR. ALEXANDER TSCHIRCH\*

#### A Tribute

THE SEVENTIETH birthday anniversary celebrations in honor of Prof. Tschirch are over and will long be remembered because of the world-wide response which they have inspired and the univer-



Prof. Dr. Alexander Tschirch

sal respect and affection expressed toward this great man, by the pharmacists of every nation. It was a beautiful tribute to the man and a striking evidence of the power of personality and service in the field of pure science, where all people find a common ground of sympathy and understanding.

The desire to do honor to this great savant of the pharmaceutical sciences was spontaneous. His researches and studies in botany, pharmacognosy, and plant chem-

istry, for over a quarter of a century, have influenced and often led, his colleagues in every country. He has only recently completed a labor of fifteen or more years, in the writing of his encyclopedic "Handbuch der Pharmakognosie" and is still in the zenith of his powers, mentally and physically.

The first celebration was with his former students who planned one of those "family reunions" which had been so delightful a feature of their University days. This was restricted to those who knew him intimately, who had been inspired by his guiding and fatherly instruction during their formative years, and they came from many parts of Europe to participate. Those who could not be present sent letters, telegrams and gifts and every feature was delightful and joyous, even the weather contributing to the event by furnishing a warm sunshiny day for an outdoor gathering and a glorious view of the snow-capped Alps.

This "family gathering," as Prof. Tschirch likes to refer to it, began on Saturday evening, October 16th, when many gathered at the Kursaal Schanzli to hear the celebrated concert orchestra. This

<sup>\*</sup>Director of the Pharmaceutical Institute of the University of Bern, Bern, Switzerland.

was entirely informal but gave an opportunity to meet and know those who had come from a distance.

October 17th was the actual birthday date and it had been reserved for the student events, the more formal University celebrations coming almost a week later. At ten o'clock on the morning of the seventeenth the auditorium of the Pharmaceutical Institute was crowded by those whom Prof. Tschirch had either trained as pharmacists or had taught something of his own analytical and creative methods of research and then sent out to carry his ideals and teachings to distant centres.

To properly understand this feature of the celebrations it is necessary to appreciate the affectionate regard with which Prof. Tschirch is held by his students and his attitude toward those who come to him for instruction. There is every evidence of sincere personal interest in the student; one need but see that kindly smile and the paternal regard with which, from day to day, he follows the progress attained, to realize that here is a true teacher.

Then an important part of the academic year has always been excursions and as those have often been botanical they naturally led the teacher and students toward the wonderful mountains and valleys so close to Bern. In motoring this summer with Prof. and Mrs. Tschirch through much of this beautiful country it seemed that every village, valley or mountain recalled some student excursion or dinner of past years, and, from my personal experience on two such excursions during the last semester, they must all have been notable events.

Always Prof. Tschirch is the center of interest, keenly alive to every incident of the trip, overflowing with accounts of travel or experiences when the opportunity arises, ready of wit, joining in and even leading the singing, so delightful a feature here of every student gathering, and fully enjoying the humorous happenings so sure to occur.

The first event of the celebrations was reminiscent of these excursions. Pictures were reproduced on the screen representing many occasions and including many well-known persons and many interesting and amusing incidents.

Following this, all assembled at the Bellevue Palace, Bern's most beautiful hotel, for the big event of the day. About eighty were present for dinner and telegrams and letters were also there from almost every former student unable to come personally. (Over 300

letters and telegrams were received from individuals and official communications from forty-six scientific societies.)

At the dinner the interesting European custom was followed of calling for speeches between courses and while this extends the dinner for several hours it has advantages. Among those speaking were Dr. Gustav Voda, of Czechoslovakia; Prof. Casparis, of Basil,



TSCHIRCH "HONOR" WINDOW.

Switzerland and representatives of Swiss, German and French societies of pharmacists, pharmacognocists and chemists.

The outstanding features of the morning was the presentation to Prof. Tschirch, by the students, of an art-glass window (50 x 75 cm.) which symbolized a medieval teacher of science, surrounded by his pupils who are being instructed in the mysteries of the poppy

plant. The design was by Albin Schweir and the art-glass work by Louis Halter, noted Swiss artists. A reproduction in four colors (15 x 21 cm.) has been presented to those who participated in the gift and a limited number of copies are still available and should find a place in every college of pharmacy in America and in many professional pharmacies where it will always suggest the antiquity and dignity of the calling.

Finally the time came for Prof. Tschirch to respond, which he did with his characteristic forcefulness but with affection and humor. The frequent assembling of those at the dinner near the chair of the guest of honor that they might "drink to his health," the frequent "hoch," and the final gracefully and gallantly presented toasts to each lady present, by Prof. Tschirch as he passed around the tables, were new customs to Americans, but were truly expressive of the fine feeling of friendship evidenced throughout the celebrations.

The many gifts, including the beautiful flowers, were taken to the home of Prof. Tschirch, after the dinner and outdoor coffee, and through the following week open house prevailed and many persons

called to offer congratulations.

On the following Saturday, the twenty-third, came the formal reception under the auspices of the Medical Faculty of the University of Bern (in Bern the Pharmaceutical Institute is a division of the Medical School of the University). The dignitaries, in formal dress, assembled at 10.30 in the Pharmaceutical Institute which was decorated with flowers. Prof. Burgi, Dean of the Medical Faculty, presided and, after extending the congratulations of the Government of Switzerland, of the Canton of Bern, and the Medical Faculty he presented a life-size, bronze, bas-relief of the bust of Prof. Tschirch, as a gift from the University.

Prof. Dr. Thoms, of Berlin, then presented the "Festschrift," a subscription volume of about 500 pages, published by Tauchnitz, of Leipzig, and containing original contributions to science from

the friends and students of Prof. Tschirch.

Then followed many brief addresses, most of them accompanied by engrossed and beautifully illuminated resolutions of congratulations. Among those speaking were the Rector Magnificus of the University, Dr. Mayne; Prof. Kohlschütter, Professor of chemistry in the University of Bern, representing the Deutsche Chemische Gesellschaft; Prof. E. Fullerton Cook, representing the United States Pharmacopæia and the Philadelphia College of Pharmacy and Science and also presenting a communication from Prof.

Eberle for the American Pharmaceutical Association; Dr. Winkler, of Austria, who presented honorary membership in the Society for Historical Pharmacy; Prof. Kofler, of Austria, speaking for the pharmacognocists of the world; Dr. Salzmann, of Berlin, of the Deutscher Apotheker Verein, which had placed a tablet on the house, which was the parsonage, where Prof. Tschirch was born, in the little town of Guben, Germany; Prof. Dr. Thoms for the Deutscher Pharmazeutische Gesellschaft; Dr. Firbas, speaking for the Austrian pharmaceutical associations, and many others, representing pharmaceutical, chemical and botanical societies of Switzerland.

The honorary degree of "Doctor of Engineers" was awarded by the Technical University of Stuttgart and the degree of "Doctor of Natural Sciences" by the Technical University of Zurich. The "Alfred Werner Medal" for original researches in chemistry, was awarded by Prof. Karrer for the University of Zurich. Prof. Tschirch was also made a life member of the Veteran Druggists'

Association of New York.

Prof. Tschirch responded to these many speeches by a few words of thanks and appreciation, specifically referring to each address which had preceded, then briefly reviewed his life and accomplishments.

A fitting culmination of the events was the banquet in the evening when many who had spoken in the morning and others were called upon for a few words, Prof. Tschirch responding appropriately. The banquet was less formal than the University exercises of the morning and many opportunities were given for colleagues and friends to tell of incidents and experiences, often amusing, which had marked their long and interesting friendship with the guest of honor, he, in turn, responding with equal good humor and repartee.

An important feature of every celebration, not to be overlooked, was the recognition given Frau. Prof. Tschirch who has always been of great assistance to her husband, helping him in varied capacities and endearing herself to all with whom she comes in contact.

The seventieth birthday celebrations are over and they have left an international sense of amity and good will; they have also brought great gratification to one who deserves every honor pharmacy can bestow. The universal wish is that many more years may be granted to Prof. Tschirch that he may further enrich the world by his inspiration and contributions.

E. FULLERTON COOK.

r

### DR. GEORGE D. ROSENGARTEN

R. GEORGE D. ROSENGARTEN has been elected president of the American Chemical Society, to assume office on January I, 1927, succeeding Prof. James F. Norris, of the Massa-

chusetts Institute of Technol-

ogy.



Dr. George D. Rosengarten

Dr. Rosengarten was born in Philadelphia on February 12, 1869. He was a special student at the Philadelphia College of Pharmacy in 1884, and was graduated from the University of Pennsylvania with the degree of Bachelor of Science in 1890, and received a Ph.D. from the University of Jena, Germany, in 1892. He was with Rosengarten & Sons, 1893-1901, and was its vice-president, 1901-When Rosengarten & 1905. Sons amalgamated with Powers & Weightman, in 1905, to

become the Powers-Weightman-Rosengarten Company, and later, Powers-Weightman-Rosengarten, Inc., he became vice-president of the company.

He has been a director of the American Chemical Society since 1919, and is now a member of its executive committee. 1911-12 he was chairman of its industrial division and from 1915 to 1922 a councillor-at-large. He is a former president of the American Institute of Chemical Engineers, and a fellow of the American Academy of Arts and Sciences. He is a member of the Board of Trustees of the Philadelphia College of Pharmacy and Science, Committee of Revision of the United States Pharmacopoeia and American Philosophical Society, and a director of the Franklin Institute.

His social activities are represented by membership in the following clubs: The Franklin, Racquet, and Rittenhouse of Philadelphia; the Cosmos of Washington, and the Chemists Club of New York.

Dr. Rosengarten has been president of his class at the University of Pennsylvania since 1918. He was chairman of the finance committee of the 1926 Golden Jubilee Meeting of the American Chemical Society held in Philadelphia in September last.

Quietly, modestly and unostentatiously, he exerts an important influence in promoting the development of the American chemical industry, while his gracious personality has endeared him to a wide circle of friends.

J. W. ENGLAND.

# ABSTRACTED AND REPRINTED ARTICLES

### NOTE ON THE DIETHYLPHTHALATE TEST\*

By H. Wales (Drug Control Laboratory, Bureau of Chemistry, Washington, D. C.)

THE USUAL tests for diethylphthalate depend upon the sapon-ification of the ester and condensation of the resulting o-phthalic acid with a phenol. Both the U. S. Pharmacopœia 1 and the Bureau of Internal Revenue 2 tests for diethylphthalate depend upon the condensation of the o-phthalic acid with resorcinol to produce a dye of high fluorescent power. The only specific reference found in the literature to a test for diethylphthalate in drug products is to a work done by Eilles,3 who describes a different method and merely mentions that fluidextracts and tinctures should be clarified with lead acetate before the test is made.

Many crude drugs contain derivatives of naphthalene, anthacene, or phenanthrene, all of which may be oxidized to o-phthalic acid. Theoretically such preparations when tested for phthalates might give positive results, as was found to be the case with a number of products believed to be made with pure alcohol. The decomposition of the plant material probably proceeds slowly, as a freshly prepared tincture of hyoscyamus failed to give a positive test for

<sup>\*</sup>Reprinted from Jour. A. O. A. C., Vol. IX, No. 4, p. 476.

<sup>&</sup>lt;sup>1</sup> U. S. Pharmacopœia, p. 353.

<sup>&</sup>lt;sup>2</sup> Appendix to Regulations No. 61. Formulæ for completely and specially denatured alcohol. Revised September 21, 1923, p. 13.

<sup>&</sup>lt;sup>2</sup> Z. Nahr. Genussm., 1923, 45:379.

phthalate, while several that had been prepared for some time gave the test. It is apparent, therefore, that some method must be used to remove these interfering substances before the test for phthalic acid derived from diethylphthalate can be made.

On applying the lead acetate clarification to several products, as suggested by Eilles, it was found that positive tests were still obtained in some cases. However, basic lead acetate did remove the interfering substances when used as described and did not remove diethylphthalate from products containing traces of this compound.

The following procedure, which embodies the essential features of the published methods, has been found to give satisfactory re-

sults:

#### Method

To such a quantity of the preparation as contains about 10 cc. of alcohol add an excess of basic lead acetate solution, U. S. P., and filter; then add an excess of solid sodium carbonate to precipitate the lead, filter, and extract the filtrate with 15-20 cc. of petroleum benzine. Add 0.2 cc. of approximately 10 per cent. sodium hydroxide to the benzine extract and evaporate to dryness on the steam bath. Add to the residue 5 cc. of concentrated sulfuric acid and warm on the steam bath for several minutes to convert the phthalic acid to anhydride. Add 25 milligrams of resorcinol and warm to effect solution. Transfer to a clean dry test tube and heat in a paraffin bath at 160°-170°C. for 10 minutes. Pour the cooled melt into 150 cc. of water and make alkaline with approximately 10 per cent. sodium hydroxide. If diethylphthalate is present, a greenish yellow fluorescence appears at once and persists indefinitely without fading.

Wash all glassware with soap and rinse several times with alcohol before using. If porcelain dishes are used for the evaporation, heat first to redness. As a precautionary measure, run a blank. In all cases in which fluorescence is observed allow the solutions to stand 36-48 hours before reporting the presence of diethylphthalate, thus guarding against any pseudo fluorescence.

#### Discussion of Results

Several of the products examined formed very bad emulsions with petroleum benzine, and some material which gave a pseudo

fluorescence that did not fade completely for two to three days was carried through. In these cases it was found necessary to make a preliminary distillation. The distillate containing the alcohol, diethylphthalate, and other volatile substances present was then treated with basic lead acetate and subjected to the test. In fact, in every instance where a positive test is obtained the writer believes that as an additional precaution the result should be confirmed by distilling some of the product under examination and preparing the test.

The following fluidextracts and tinctures, many of which give positive tests for phthalates by the usual methods, have been examined by the proposed method with negative results; belladonna, black haw, buchu, cascara sagrada, cinchona, colchicum, digitalis, gelsemium, hyoscyamus, ipecac, licorice, nux vomica, senega and squill.

# Summary

A fluorescence obtained from drug products by either the petroleum benzine extraction method or the distillation method does not prove the presence of diethylphthalate unless interfering substances are removed by means of basic lead acetate. Even then a positive result, when obtained by the extraction method, should be confirmed by distilling some of the product under examination and applying the test on the distillate after first treating it with basic lead acetate.

# ANILINE DYES IN THE TREATMENT OF INFECTION\*

By John Churchman

Professor of Experimental Therapeutics, Cornell University Medical College, New York, N. Y.

A N IDLE question not infrequently put to those working in this field—"Will an ideal antiseptic ever be discovered?"—suggests two other questions not so idle since they strike at the heart of the problems with which the investigation of the therapeutic possibilities of the aniline dyes is concerned. It leads us to ask ourselves, first, what are the defects of the antiseptics at present in use; and second, what would be the characteristics of an ideal antiseptic?

<sup>\*</sup>Reprinted from Journal Industrial and Engineering Chemistry.

Certainly there is no lack of chemical agents which are capable of killing bacteria. The fundamental objection to them is twofold. Either they are so highly toxic to all forms of protoplasm as to find only restricted application in therapeutics, or, because of their toxicity or for other reasons, they cannot be brought into contact with the bacteria which must be reached.

An ideal antiseptic would therefore first of all be a substance which, though strongly antagonistic to bacteria, would be almost or quite non-toxic to animal cells in doses lethal for microörganisms. The use of such a substance would not be restricted to surface infections, but could be introduced into the tissues themselves or even into the circulation and thus really reach the bacteria which are causing the trouble.

An ideal antiseptic would also have powers of penetration so that it could distribute itself beyond the point of application, or, if injected into the blood stream, percolate throughout the tissues.

An ideal antiseptic would not cause any reaction of coagulation in the animal cells or humors which would impede its own progress, as bichloride of mercury, for example, does. Nor would its bactericidal activities be hindered by the presence of serum or other animal substance in whose presence the agent must of necessity function.

An ideal antiseptic would persist in the tissues long enough to accomplish its purpose and be quickly eliminated after its bactericidal work was over. It would be equally effective against all types of bacteria, against the heat-resistant spore as well as against the delicate gonococcus.

It would, of course, be fatuous to hope and rash to predict that any one substance will ever be found combining all these desirable qualities. Yet the fact that investigation has actually succeeded in overcoming some of the apparently insuperable difficulties, and in providing substances which in some respects begin to approach our ideal, justifies a certain optimism as to the remaining obstacles.

In this struggle to put the treatment of infection on a sound and scientific basis investigation of the bactericidal properties of the aniline dyes has played an important part, and it is within the last decade that they have aroused most widespread interest. The outbreak of the war stimulated—as wars always stimulate—an interest in the treatment of infected wounds, not particularly active in years of peace; and from 1914 on, the painstaking investigations of preceding years were precipitated by the acid of necessity as the salt of results.

# History of Aniline Dyes in Medicine

It is, of course, never possible in science—since the advance of one year issues always from the work of the preceding years—thus to segregate any one decade, and if we wish to date the birth of aniline dyes as therapeutic agents we must go back of 1914 many years. We must go back to Ehrlich's observation on the selective activity of methylene blue made years ago. Ehrlich noticed that this dye when injected into the circulation exhibited a sharp selective activity, staining only the nerve cells. The fact made an indelible impression on his mind. Though he doubtless at the time had intimations of its far-reaching significance, he was forced by circumstances for the time being to abandon the line of thought which the observation suggested. But he never ceased to brood over it. And several years later he was able to turn it to account by making the brilliant therapeutic discovery of salvarsan and by founding a new science.

The science which he founded is the science one branch of which is at present our particular concern. The theory of chemotherapy which Ehrlich advanced and so brilliantly supported was simple. enough. Indeed, like many such new hypotheses, it was, as now appears, too simple. It posited first the doctrine of specific chemical affinities and advanced to account for them the diagrammatic. possibly fantastic, machinery of chemoceptors. It taught, therefore, that successful antiseptic therapy must be highly selective. It taught also that substances could be found or constructed lethal for invading organisms though tolerated by the infected animal, and that the trick was to find or devise the substances and to determine the dose. It advanced the doctrine of a therapia sterilisans magna—the idea. that it is highly desirable if not essential to destroy all the invading organisms at one blow and that to accomplish less than this is to accomplish nothing. It conceived the problem of infection largely from the standpoint of blood infection and assumed that the effective contact between drug and micro-organisms took place in the blood stream—a therapia sterilisans magna accomplished within the blood vessels. It finally advanced the theory, and demonstrated its correctness by brilliant success, that the proper procedure in this field was to start with some molecule whose properties appeared promising and then by chemical manipulation through processes of substitution to mold its selective capacities more nearly to the ideal and fit it for use in a therapia magna.

Very briefly put, these are the ideas which have dominated this field of experimentation in the period during which the aniline dyes have been the subject of intensive therapeutic investigation. But the antagonistic action of the dyes toward microörganisms had been attracting the attention of observers for years before these ideas had entered the scene. Robert Koch, who grasped the whole problem of infection with extraordinary accuracy and vision, and who brought to its solution an exact experimental method that has never been surpassed, was well aware that some of the aniline dyes "killed" or inhibited bacteria, and foresaw the possibility of their application in the treatment of infection. Such an application was indeed made on a fairly extensive scale by Stilling in 1890. But it was an unfortunate adventure since Stilling, with none too accurate a conception of the problem with which he was dealing, claimed and expected much more than the facts justified and the aniline dyes fell into deserved disrepute. The demonstration, however, by Conradi and Drigalski in 1902 that certain triphenylmethanes (crystal violet) could be used to advantage in the selective cultivation of bacteria in pure culture in the laboratory, and the brilliant chemical and protozoöcidal studies being published by Ehrlich and his school on the therapeutic effects of trypan red, atoxyl, and their modifications kept up a vivid interest in medicine in the aniline dyes. Shortly before the war, in Frankfort, the bactericidal properties of the acridine dyes were demonstrated. Browning tested them out clinically and later was responsible for their wide and on the whole encouraging use in the British Army during the war. About the same time other English observers were becoming enthusiastic about the antiseptic properties of brilliant green.

ļ

t

1

S

In 1912 I first called attention to the peculiar properties of gentian violet and related triphenylmethanes and brought out the fact that the bactericidal or, to use the more correct term which I at that time introduced, bacteriostatic behavior of these dyes closely paralleled the Gram reaction. Bacteria are rather sharply divided into two large groups. One of these groups, the Gram positives, when stained with basic triphenylmethane dyes which are afterward fixed with iodine, retains the dye after immersion in alcohol; while the other group, the Gram negatives, gives the dye up when the alcohol is applied. It was shown in my laboratory that it is exactly the Gram positives which are as a rule most susceptible to gentian violet and exactly the Gram negatives which are least susceptible. Stray obser-

vations of this parallelism had doubtless been made before, but its significance had not been appreciated and the parallelism had not been shown to be at all general by the demonstration that it held, with a small percentage of exceptions, throughout the bacterial field. In 1923 the reverse selective power of acid fuchsin and other dyes was first reported from my laboratory. It was found that these substances exhibited a selective power that was in some respects the exact opposite of that of gentian violet. As between Gram-positive spore-bearing aerobes and Gram-negative bacilli, gentian violet and acid fuchsin act in an opposite manner. This observation threw a somewhat new light on the whole problem, and from it was developed the new mixture, now called acriviolet, which has received a certain amount of encouraging clinical trial and of which something will be said later.

In 1919 mercurochrome was produced in the laboratory of H. H. Young in Baltimore. This substance is a combination of fluorescein and mercury. It is similar to, though perhaps not identical with, a substance produced in Germany several years ago. It represents an attempt to attach a strong but non-penetrating antiseptic (mercury) to a penetrating dye and thus to impart to one portion of the molecule the virtues of the other part.

# Application in Bacteriostasis

With this brief sketch of the story of the aniline dyes in medicine in mind and with the principal dates fixed, we are in a position to examine the applications which have been made of them and to pass to an inquiry as to their place in the modern conception of chemotherapy and their probable future.

IN LABORATORY PROCEDURES—This phase of the subject is often overlooked in focusing the gaze on the somewhat more spectacular therapeutic aspects. Vital staining with methylene blue was the initial observation from which the science of chemotherapy really sprang. This was a new conception in medicine. The dyes had long been used to stain dead tissues and thus render the finer structures of the cell visible. From their use had grown the sciences of histology and cellular pathology. But it would hardly have been suspected until experimental demonstration of the fact was furnished that aniline dyes could be introduced into the cell and that life in the cell would continue. Whether the living nucleus can be stained is

still a matter about which there is no general agreement. Experiments of my own made in 1914 seemed to indicate that even the living nucleus can be stained. But as this observation was not followed up owing to the exigencies growing out of the war, and as the observation has not been confirmed by others, the question must still be regarded as an open one.

That the protoplasm of the living cell can be stained by dye injected in to the circulation is, however, a matter not open to doubt; and one of the most important contributions made in this field has been the development of a new method for the study of cellular activity; that is, the method of vital staining. In recent years a technic has been developed by which it is possible to inject single cells, under the microscope, and it is not at all out of the question that investigations by this method may throw altogether new light on the micro-chemistry of the cell and thus on its ultimate nature. would, of course, be of fundamental importance, for the nearer we come to an understanding of the physiology of the cell the nearer we approach the secret of life itself. Certain limitations of study by this method brought out by experiments from the writer's laboratory will have to be borne in mind. These experiments demonstrated the existence of a communal activity among bacteria and show that we cannot argue from the behavior of single cells to their behavior in groups.

Another field in which the dyes have been of importance in the laboratory is in the application of their selective inhibitory properties to the cultivation of bacteria free from contaminations. work of Conradi and Drigalski has already been mentioned. One of the very difficult problems in bacteriology is the separation of the typhoid bacillus from contaminations with the closely related colon bacillus. This separation is of the utmost practical importance and Conradi and Drigalski showed that by incorporating crystal violet into the media on which the suspected material was grown the separation could be accomplished, since the dye, when used in proper proportions, prevents the development of B. coli while allowing B. typhosus to grow. My own early observations were concerned with a selective differentiation of B. subtilis and B. prodigiosus by means of gentian violet and throughout the work this selective bacteriostasis has been stressed and numerous examples of it observed. It is a property of the utmost interest and importance. The dyes in bringing about this inhibition do not necessarily kill the organisms. They do not necessarily alter their nature. All they appear to do is to paralyze the reproductive mechanism. And once the bacteria are removed from contact with the dye, reproduction may proceed normally. The writer has succeeded in prolonging this reproductive paralysis for many days. For example, in one experiment B. anthracis was stained with gentian violet and then injected into the highly susceptible mouse. The controls always died of anthrax within thirty-six hours. But the mice receiving stained organisms survived several—in one instance twenty-six—days in perfect health only to die eventually of anthrax.

By reason of the parallelism between the Gram reaction and the gentian violet reaction it is the simplest matter in the world to separate many of the Gram-negative organisms from contaminations with many of the Gram positives by streaking the mixture of the two organisms on gentian violet agar or by staining the mixture with gentian violet and streaking on plain agar. But more than this is possible. As already indicated, the writer first demonstrated in 1912 the phenomenon of reverse selective bacteriostasis by showing that acid fuchsin possessed, under particular experimental conditions, a selective bacteriostatic power that was in some respects the reverse of that of gentian violet since it had a greater affinity for Gram-negative organisms than for Gram-positive spore-bearing aerobes. In this publication it was shown to be possible by a particular technic to separate from a mixture of Gram negatives and certain Gram positives either organism desired, in pure culture, by the use of either acid fuchsin or gentian violet. This demonstration of the two types of selective bacteriostasis, normal and reverse, indicates the wide possibilities of the method, for substances may ultimately be found which will make it possible on the same principle to separate from each other any two organisms whatsoever.

CLINICAL APPLICATION—One practical clinical application of the phenomenon of selective bacteriostasis will be cited. Cultivation of *B. tuberculosis* in pure culture has always presented great difficulties because the material in which the organism is usually sought (sputum or feces) is always heavily loaded with other organisms which overgrow *B. tuberculosis*. The majority of these contaminating organisms are readily inhibited by gentian violet while the growth of *B. tuberculosis* is little affected by this dye. On the basis of the writer's observation, therefore, Petroff in 1915 devised a medium,

now widely used, in which gentian violet is incorporated and on which the contaminating organisms do not grow though *B. tuberculosis* grows well.

# Experiments in Chemotherapeutics

It is of great importance to bear in mind that the early experimental studies in the chemotherapeutic field were done largely, not with bacteria, but with Protozoa. It was with organisms of this group that the remarkable series of experiments which began with trypan red and ended with salvarsan were made. This story is doubtless familiar-how Ehrlich, first interested in the vital staining properties of methylene blue, developed with Weinberg the parasitocidal substance trypan red, how he then became interested in atoxyl and other arsenic compounds, how by a brilliant series of experimental manipulations of the molecule he arrived at the drug so useful in the treatment of syphilis. While these epoch-making investigations were in progress many attempts were being made to parallel in the bacteriological field the successes being obtained in the protozoan field. The early optimism with which these studies were conducted was followed by pessimism when it was found, much to the disappointment of those who had expected the protozoan results to be readily duplicated, that conclusions drawn from experiments with Protozoa did not hold true for bacteria; and many felt that chemotherapy of the Ehrlich type had no future for infections caused by bacteria. The European war re-awakened a wide interest in the whole problem of infection; and, coming as it did, just at the time when laboratory studies with acriflavine and gentian violet were again arousing interest in the aniline dyes, these substances at once began to play a part in the desperate battle with infection which medicine, faced with the colossal crop of infected wounds which the war produced, had to wage. This interest did not subside at the Armistice. On the contrary, studies of the aniline dyes and their possible use in the treatment of infection have been carried on with renewed vigor. These studies have beyond doubt led to a distinct advance in this field and there seems to be considerable reason for expecting that their continuation will lead to a solution of the knotty and hitherto insoluble problems of the treatment of bacterial infections in the blood stream.

# Types of Infection Amenable to Dye Antisepsis

Five dyes have attracted chief attention: acrifiavine, brilliant green, gentian violet, mercurochrome, and acriviolet. Data are not at hand to discuss the highly complex question of the relative merits of these substances. We must satisfy ourselves by stating that all five are of some value and by indicating the types of infection in which dye antisepsis has been achieved.

The dyes lend themselves readily to use in the treatment of surface infections. It is here that some features of their superiority to other antiseptics come particularly into evidence. The dyes are non-irritating to many of the body surfaces (the urethra and bladder appear to be exceptions to this rule) and they have a certain power of penetration, particularly for epithelium. They persist also and are thus able to perform their function of bacteriostasis on body surfaces over a fairly long period of time. Above all, on surfaces where they can be used at all they do little or no damage. They cause little or no destruction of body cells. They do not coagulate blood or humors and thus erect barriers against their own action.

The behavior of the aniline dyes in the treatment of surface infection may be illustrated by reference to a few cases. After the war a serious problem was presented in American army hospitals by the infection of many amputation stumps with the diphtheria bacillus. This organism is quite susceptible to gentian violet. The writer therefore treated at the Walter Reed Hospital in Washington a number of such cases by staining the stumps with gentian violet after meticulous mechanical cleansing. These stumps were in this way readily freed of the bacillus of diphtheria. I was able also to demonstrate clinically the action of selective bacteriostasis since, although it was impossible to sterilize other stumps infected with the Gramnegative colon bacillus, the cases in which the diphtheria bacillus was the offending organism were promptly cured. We have also been able to sterilize with gentian violet a number of infected knee joints. A boy was admitted to the hospital two weeks after an elevator accident with a dirty granulating wound near the left knee cap, a knee joint full of pus, and a comminuted fracture of the patella. The organism responsible for the infection was the Gram-positive staphylococccus aureus. The combination presented by this case offered a difficult surgical problem, since to let the patella go unsutured, leaving the patient with permanent non-union, would mean a bad deformity, while to attempt to suture it in the presence of infection involved great risk. We were able in this instance by means of gentian violet introduced into the knee joint, using a special technic already described, to sterilize the joint so that we could open it up and proceed with the suture. Perfect union resulted and the patient left the hospital with a normal leg. I have recently in similar fashion sterilized the vagina in a case of gonorrheal endocervicitis.

The aniline dyes are, as we therefore see, coming into use in the treatment of surface infections. In many places, acriflavine and mercurochrome have already replaced iodine for many of the conditions for which the latter has always been used; and it is not unlikely that these will be replaced by acriviolet, a dye which is in many if not in all respects superior to either.

Brilliant green and gentian violet belong to the triphenylmethanes and acriflavine to the acridines, and that is about all that it is necessary at the present time to say about them. But of the chemistry of acriviolet and mercurochrome an added word will not be out of place.

The idea that a weakly bactericidal but penetrating substance like a dye might be combined with a strong antiseptic, with no penetrating power, and the virtues of both be thus made available has long tempted workers in this field. A number of combinations have been made, including a combination of mercury and a fluorescent dye such as that used in mercurochrome. This was rediscovered by Young and his co-workers, improved and brought into general use; and it has proved of great value.

Acriviolet represents an effort in a somewhat different direction. When the reverse selective action of acid fuchsin was first observed the obvious next step was to combine two substances of different selective powers and thus to fortify the weakness by one by the strength of the other. Acid fuchsin and gentian violet will not mix. But acriflavine and gentian violet, two dyes of somewhat different selective powers, will, and acriviolet is the name given to this mixture. This dye has received test on a fairly wide scale and, within the limitations to which all substances of this sort are subject, appears to have a distinct value.

The great desideratum in this field is the development of a method by which we can treat infections successfully via the blood stream and particularly infections which are being spread by the blood stream—that is to say, blood poisoning. At the Baltimore Meeting of the Society I discussed in some detail the relation of the

dyes to this question. Allow me merely to state the conclusions which I had at that time reached and which I have seen no reason to alter since. So far as the evidence from animal experimentation goes, there is little or no reason to believe that injections into the circulation of aniline dyes or any other substance now known will kill bacteria floating in the blood stream. In this respect bacterial and protozoan infections differ sharply. On the other hand, there is a considerable body of evidence at hand from clinical sources which strongly suggests that certain substances, more particularly gentian violet and mercurochrome, may considerably alter the course of a septicemia. Unfortunately, this evidence has not been subjected to a sufficiently critical analysis to enable us to determine its value; and in the absence of control experiments on a large scale it is impossible at the present time to reach a definite conclusion. The wide interest in both laboratory and clinic which the aniline dye studies have stimulated in the treatment of septicemia makes it not unlikely that important advances will be made in this field in the near future.

### Relation of Molecular Structure to Bactericidal Power

One cannot speak of subjects which engaged so much of Ehrlich's attention without touching on the idea so dear to his heartnamely, the relation of molecular structure to bacteriostatic power. The parallelism between the selective activities of the triphenylmethane dyes and the Gram reaction, which must itself be dependent on the physical or chemical structure of the Gram negative and Gram positive groups of bacteria, suggests at least a point of attack for this investigation. By following leads of this kind it may be that we shall arrive at a closer understanding of the chemistry of bacteria as well as determine what portion of the dye molecule is responsible for its bacteriostatic characteristics. When the reverse selective power of acid fuchsin was first observed it was thought that the sulfonic acid group, the only group in acid fuchsin not found in basic fuchsin, might be responsible for the reversal of selective power. This second even more probable since simpler sulfonated substances, ethyl sulfate and H-acid, also exhibited reverse selective action. But it was unfortunately found that other substances, such as acriflavine, which contained no SO<sub>3</sub> group, also possessed reverse powers. We cannot at present, therefore, be said to know much concerning the relation of molecular structure of the dves to selectivity beyond the idea which generally obtains and which appears to rest on considerable body of evidence—that these bacteriostatic powers are bound up with the basic auxochromic groups.

#### Therapeutic Properties of Dyes

What are the qualities of the aniline dyes observed in studies of the kind we have been discussing which justify their present adoption and the expectation that out of the investigation will come discoveries of therapeutic importance? The aniline dyes provide us first of all with an admirable machinery for the study of the microchemistry of antisepsis. By their incorporation in media or in other ways we are able to manipulate bacterial growth somewhat at will and up to a certain limited point to control some of the processes of bacterial life. Thus we may put the brakes on sporulation and keep a sporulating organism for many days in the vegetative form by keeping it exposed to acid fuchsin.

The dyes have a penetrative power for epithelium, at least a not inconsiderable penetrative power. Though not very strongly bactericidal, they are, even in weak solutions, highly bacteriostatic, and their study has brought out the importance in therapeutics of this somewhat new conception of bacteriostasis (a direct development of the gentian violet studies) which appears to be leading us away somewhat from the Ehrlich conception of the necessity of a *sterilisans magna*.

The dyes are less toxic for many animal cells than they are for bacteria; they appear to be pretty well tolerated even by the blood stream.

#### Conclusion

In stating these qualities of the aniline dyes I have answered the questions put at the beginning of this paper as to the relation of the dyes to the ideal antiseptic and have indicated the probable course of future development in this field. It seems hardly likely that this development will occur without considerable modification in the underlying conceptions of chemotherapy. Reference has already been made to the significance of the idea of bacteriostastis for the theory of a sterilisans magna. Much skepticism has arisen also as to the existence of chemoceptors, and the allied hypothetical machinery of affinities. Even the idea that the effective contact between chem-

ical substance and microorganism takes place in the blood stream is now open to considerable doubt. But however these conceptions of Ehrlich are modified, or even if they are ultimately abandoned, they have represented one of the greatest advances in the history of medicine. They provided a new starting point. From this starting point investigation of the aniline dyes has proceeded a considerable distance. It promises to go much further in the near future.

# TABLOID TALES OF THE PROGRESS OF SCIENCE IN 1926

CHEMISTRY—Hydrogen was transmuted into helium by Prof. F. Paneth and Dr. Peters of Berlin University.

Gold was claimed to have been transmuted to mercury by Dr. A. Gaschler, of the Berlin Technical High School.

Nitrogen is changed to fluorine and then to hydrogen and oxygen when hit by the nucleus of an atom of helium, Dr. William D. Harkins, of the University of Chicago, told the National Academy of Sciences.

Prof. S. B. Hopkins, of the University of Illinois, discovered a new chemical element, No. 61 in the periodic table, and named it illinium.

Elements 75 and 43, reported discovered by Prof. Walter Nod-dack, of Berlin, in 1925, have been relegated to the limbo of still undiscovered metals, by experiments at the Platinum Institute of the Russian Academy of Sciences which failed to substantiate the German results.

A synthetic drug called plasmochin, more powerful than quinine, was made in the Elberfelder Farbenfabriken.

Compounds analogous to chaulmoogra oil were made in the laboratory by Dr. Roger Adams of the University of Illinois and were found to act as an effective germicide against leprosy.

The valuable constituent of insulin was prepared in crystalline form by Dr. John J. Abel, of Johns Hopkins University.

The first enzyme, one of an important class of substances involved in digestion, to be isolated was made in a crystallized form by Dr. James E. Sumner at Cornell University Medical School.

An extract of the parathyroid gland, which controls the lime

content of the blood, was prepared successfully from animal glands by A. M. Hjort and H. B. North, Detroit chemists.

Luminous flames radiate more heat than non-luminous flames, according to tests made by Prof. R. T. Haslam and M. W. Boyer, of the Massachusetts Institute of Technology.

A new method of welding pieces of metal together was announced by Dr. Irving Langmuir, of the General Electric Company, by which hydrogen molecules are broken into atoms and recombined to give an intensely hot flame.

Methods for liquefying coal and obtaining motor fuel and other valuable products from coal were perfected by Dr. Friedrich Bergius and Dr. Franz Fischer, both Germans and General Georges Patart, of Paris.

A process for making sugar from wood was developed by Prof. Freidrich Bergius of Heidelberg University.

Tests made by government chemists showed that a thin film of metallic chromium electroplated upon printing plates of finished steel or copper-nickel would make the plates wear longer than plates of hardest steel.

A world famine in rubber by 1930 was predicted by the U. S. Department of Commerce.

Commercial application of carbon dioxide ice for refrigeration purposes has reached the practical stage.

The widespread supplanting of cotton by rayon and similar fabrics made from wood began a revolution in American agriculture.

A project was set on foot to produce levulose sugar in large quantities from the roots of dahlias.

A system of zoning was evolved at the International Conference on Oil Pollution in an attempt to solve the problems arising from the discharge of waste oil by vessels at sea.

A set of world standards for gasoline and other liquid fuels was proposed at the meeting of the International Union of Pure and Applied Chemistry.

MEDICINE.—Partial immunization to measles, by means of injections of blood serum from persons who have had the disease and recovered, was claimed in a report to the League of Nations Health Committee.

The germ of oroya fever, or Peruvian fever, was isolated at the Rockefeller Institute by Drs. Hideyo Noguchi and T. S. Battistini.

Dr. E. B. Krumbhaar of Philadelphia, announced the discovery that the spleen is an important source of the anti-bodies in the blood, which aid the body in resisting bacterial infection.

A skin test for susceptibility to infantile paralysis was originated by Dr. Edward C. Rosenow, of the Mayo Foundation.

Bacteriophage, the enemy of germs, discovered by Dr. F. d'Herelle, was declared by him to be a living parasite of parasites and not just a chemical factor.

Cause of creeping eruption was found to be a small parasitic thread worm by experts at U. S. Bureau of Entomology.

Mrs. Margaret R. Lewis, of the Carnegie Institution, and Howard B. Andervont, Johns Hopkins University graduate student, discovered that a form of cancer occurring in chickens is the result of the white blood cells running wild.

Experiments on 50,000 mice by Dr. Maud Slye, of the University of Chicago, showed that resistance as well as susceptibility to cancer in mice is hereditary.

Virus from chicken sarcoma was found to be absolutely resistant to X-rays by workers at Cancer Research Laboratory at Middlesex, England.

Rat bite fever was found to be an effective cure for general paralysis or paresis.

The Pasteur Institute claimed that babies may be protected from tetanus infection by giving prenatal doses of tetanus antitoxin to mothers.

Indications were found that trachoma, a disease of the eye for which immigrants have been barred from entering the United States, is due to a deficient diet, by Dr. B. Franklin Royer, medical director of the national committee for the prevention of blindness.

Two Prague scientists discovered a way of using washed animal blood in human transfusions.

By coating them with gold, Prof. H. Bechold, German scientist, made visible minute bacteria formerly beyond the power of any microscope.

Polonium, the radioactive element isolated by Mme. Curie, was declared to be of possible use in treating syphilis as a result of preliminary tests made at the Pasteur Institute.

The theory that some diseases may be the result of a partnership of two kinds of germs was advanced by Dr. Aldo Castellani, internationally known for his studies of tropical diseases.

Protection against typhoid fever by swallowing vaccine was tried out experimentally in bacteriological laboratories at the State College of Washington.

Discovery of the chemical compound in tuberculin that causes the skin reaction in persons that have tuberculosis was announced by Dr. Florence B. Seibert, of the University of Chicago, as a new step toward understanding the chemistry of tuberculosis.

The belief that the adrenal glands play an important part in the production of body heat was advanced by Dr. Charles Sajous, professor of endocrinology at the University of Pennsylvania.

It was shown that ultra-violet light is necessary for the formation of vitamin B, which prevents beri-beri and similar diseases, and of the growth-promoting vitamin A, at least to a certain extent.

Nickel and cobalt were shown to be necessary to the proper functioning of the pancreas, which prevents diabetes, by Gabriel Bertrand, of the Pasteur Institute of Paris.

The Health Organization of the League of Nations Medicine built up an epidemiological service to check the spread of infectious diseases between countries.

A drive for full birth and death registration throughout the United States was inaugurated by the American Medical Association.

Tetraethyl lead "anti-knock" gasoline was declared not unduly dangerous to health by the United States Public Health Service.

A movement to secure uniform milk ordinances for all the states was instigated by the United States Public Health Service at a conference of health authorities from the different states.

Berlin established a matrimonial bureau where candidates for marriage can receive medical and genetical advice.

BIOLOGY.—Dr. James B. Sumner, of Cornell Medical College isolated and crystallized the first enzyme, urease.

A "death whisper" consisting of highly intense "beams" of sound-waves too short to be audible, at frequencies as high as 300,000 per second, was shown by Prof. R. W. Wood and A. L. Loomis to be capable of killing certain small animals and plants and to have other strange biological effects.

The human body grows in three distinct spurts, Dr. Charles B. Davenport, of the Carnegie Institution of Washington, told the National Academy of Sciences.

A

0

th

cl

b

e

la

P

e

h

2

d

le

it

r

D

5

le

E

Eyes of an embryo chicken removed from the egg and planted in a cultural medium continued to grow and develop in "a surprisingly normal way" according to two British physiologists, Dr. H. B. Fell and T. S. P. Strangeways.

The theory that vitamins have opposites, "toxamins," which occur in certain foods and prevent proper bone formation and cause serious nervous diseases, was advanced by Prof. Edward Mellanby, of Sheffield University, in England.

An eleven-day-old human embryo, the youngest human speciment ever available for observation, was studied and described by Dr. George L. Streeter, embryologist of the Carnegie Institution of Washington.

The mystery of the giant cells in the blood, which are present in tubercular conditions and some other pathological cases, was solved by Dr. W. H. Lewis, of the Carnegie Institution of Washington, who announced that these cells are formed by the fusion of a number of white blood cells.

An international school of fisheries was inaugurated at the University of Washington.

A fly imported from Europe to help save New England shade trees from two insect pests was found to be an enemy to ninety-two other insects as well.

White pine blister rust, which has for several years been devastating the pine forests of the East, was discovered to be threatening the white pine stands of the West.

New corn-harvesting machinery was invented to combat the spread of the European corn borer.

Individual cells that have lived for as long as two centuries were discovered in Arizona cacti by Dr. D. T. MacDougal.

Plants will respond to strong light if it is flashed on them for as little as one one-thousandth of a second, Dr. F. A. F. C. Went, of Utrecht, demonstrated.

Suction powers in vegetable growth as high as 500 pounds per square inch were demonstrated by Dr. A. Ursprung, of the University of Fribourg, Switzerland.

The discovery that plants, as well as animals, have in their cells the special bits of living matter known as the sex chromosomes, was announced by Dr. Kathleen B. Blackburn, British botanist.

The popular idea that big seed are better than small ones was exploded by the experiments of Dr. Felix Kotowski, of the College

of Agriculture at Warsaw, who showed that size of seed has no effect on the size of vegetables.

The relationship that plants bear to each other as branches of the evolutionary family tree was demonstrated by means of serum chemistry by Prof. Karl Mez and Dr. H. Zeigenspeck, German botanists.

Plants living for months in hermetically sealed glass bulbs were exhibited to the National Academy of Sciences by Raymond H. Wallace, of Columbia University.

Physics.—Dr. W. D. Coolidge, of the General Electric Company, demonstrated a new cathode ray tube, with which these rays are for the first time obtained in quantity outside the tube. The effect of the tube is estimated to be equivalent to a ton of radium.

Prof. A. A. Michelson, of the University of Chicago, announced his new determination of the speed of light as 299,786 km. or 186,-284 miles per second.

Helium was prepared in solid form at a temperature of 457 degrees below zero Fahrenheit by Prof. W. H. Keeson, of the University of Leyden, Holland.

Magnetism of hydrogen atom was measured by Drs. J. B. Taylor and T. E. Phipps of the University of Illinois.

The penetrating cosmic rays vary daily with the aspect of the heavens, Dr. Werner Kolhoerster, German physicist, found.

Experiments made by means of midnight balloon ascensions in Belgium showed no ether drift, thus substantiating the Einstein relativity theory.

Dr. Roy J. Kennedy, of the California Institute of Technology, repeated the Michelson-Morley experiment and obtained no evidence of ether drift.

Experiments by Dr. Carl T. Chase, of the Norman Bridge Laboratory of Physics at Pasadena gave strong support to the Einstein theory of relativity, quite in opposition to Dr. Dayton C. Miller's results antagonistic to the famous theory.

Experiments by Dr. Rudolph Tomaschek, of the University of Heidelberg, Germany, fail to confirm the ether drift said to have been indicated by experiments of Dr. Dayton C. Miller, at Mt. Wilson, California.

Dr. G. M. B. Dobson and Prof. F. A. Lindemann, of Oxford University, showed that the temperature fifty miles above the earth is as high as that of a warm summer day.

A vacuum switch which stops immense electrical currents safely was devised in the new high-tension laboratory of the California Institute of Technology.

A new kind of vacuum tube with which electric currents can be amplified two million times was developed by Dr. Albert W. Hull and H. N. Williams working in the research laboratory of the General Electric Company.

The sound of a single atom of radium was made audible to radio broadcast listeners when Dr. H. P. Cady, chemist of the University of Kansas, amplified minute electric currents 700 billion times.

The proposition that beats of a master pendulum of great precision might be signalled throughout the world by radio, so that all telegraphic, astronomical, and radio instruments would be in exact tune with each other was urged by Albert Einstein before the League of Nations Committee on Intellectual Co-operation.—Science Service.

# MEDICAL AND PHARMACEUTICAL NOTES

Degree of Accuracy for Hypodermic Tablets Recommended.—The Contact Committees of the American Drug Manufacturers' Association and the American Pharmaceutical Manufacturers' Association have submitted recommendations on the degree of accuracy for several Hypodermic Tablets not included in their former report on this subject, according to a recent statement issued by the Bureau of Chemistry, United States Department of Agriculture, which is charged with the enforcement of the Federal Food and Drugs Act. Because of the importance of such tablets and the emergency conditions under which they are often used the manufacturers of the tablets and the officials in charge of the enforcement of the Federal Food and Drugs Act feel that the tablets should be made with the greatest accuracy possible under the most approved modern methods.

The recommendations specify the maximum and minimum limits for the active ingredients of the various tablets and give methods for assay to determine the degree of accuracy. Recommendations are made for the degree of accuracy in the following hypodermic tab1

lets: Codeine phosphate, pilocarpine hydrochloride, caffeine and sodium benzoate, caffeine, apomorphine hydrochloride, hyoscine hydrobromide, procaine, morphine and atropine, physostigmine sulphate, physostigmine salicylate, corrosive sublimate and arecoline hydrobromide. The Committee has withdrawn its former recommendations on atropine sulphate hypodermic tablets so that these tablets may be studied further. The Committees also recommend a method for the analysis of cocaine hydrocloride tablets as a substitute for the method previously proposed.

Copies of the recommendations of the Committees on the degree of accuracy for these tablets may be obtained upon application to the Bureau of Chemistry, United States Department of Agriculture, Washington, D. C.

ELIMINATION OF SUBSTANDARD DRUGS OBJECT OF NEW SUR-VEY BY BUREAU OF CHEMISTRY.—To see that potent pharmaceuticals comply with the standard of strength indicated by their labels, the Bureau of Chemistry has begun a resurvey of all the more important preparations according to a recent statement by the officials of that bureau charged with the enforcement of the Federal Food and Drugs Act.

The text of the statement follows:

"For the past two or three years the Bureau of Chemistry has been devoting special attention to the more important pharmaceutical preparations, particularly hypodermic tablets and potent galenicals, on the American market. In this investigation the pharmaceutical manufacturers have co-operated actively through 'contact committees' appointed by their associations. These committees have devoted intensive study to the methods of analysis for some of the most important pharmaceuticals, particularly medicinal tablets, and have specified what they regard as allowable tolerances for some of them. Two reports submitted by the committees have been made available to the industry as a whole.

"These have been examined by the Bureau of Chemistry samples of a representative number of the products of practically all American manufacturers of drugs of the type under investigation. The results of this investigation have shown that, while the large majority of these products are reliable and true to label, a not negligible proportion has been at material variance from their professed standards. In a number of instances where the quality of the product has departed excessively from the expressed standards, prosecution of the manufacturers was instituted. There has been no indication of any intent on the

part of any manufacturer of pharmaceutical products deliberately to adulterate his preparations. The deviations found have all been due, it is believed, to lack of adequate supervision and control.

#### Accuracy in Potent Medicines Essential

"The officials of the Bureau of Chemistry believe, and their opinion is shared by the responsible manufacturers, that in the case of medicines depended upon in emergencies and in the treatment of serious diseases no efforts should be spared to guarantee the accuracy of the dosage employed. It is usually impracticable for the physician to determine for himself whether or not a drug is of standar strength, quality, or purity. He must depend upon the manufacturer to furnish his medical supplies

correctly made.

"Not only are the patient and the physician protected by a strict enforcement of the food and drugs act, but the conscientious manufacturer also is protected against the competitor who perhaps fails to exercise proper care in the manufacture and control of his preparations. This work, therefore, has had the hearty support of the pharmaceutical manufacturing industry as a whole, and no little of the accomplishments of the past few years is attributable to this moral support and active cooperation.

#### Wider Range of Products in Resurvey

"The Bureau of Chemistry is now preparing to resurvey the entire field of pharmaceutical preparations. It is the intention to include a wider range of products than was investigated in the first survey. In addition to hypodermic tablets and galenical preparations there will be examined drugs in the forms of compressed tablets, tablets triturates, capsules, ampoules and As a result of the previous survey and regulatory action brought in connection therewith, and as a result of the splendid co-operation from the manufacturers in studying intensively many of the problems involved and adopting more effective methods of control, it is believed that variations from declared standards throughout the entire field of pharmaceuticals will be much less than were found during the first survey. However, it is the intention, because of the general warning to the trade through the developments in the first survey, which impressed upon manufacturers the necessity for revision of their manufacturing and control methods wherever inadequate, to bring legal action during the coming survey on variations from standards whenever these are wider than warranted under adequate supervision. It is possible, therefore, that action may be taken in some cases which would have been passed over with a warning during the former survey.

"The ultimate purpose of this work is to eliminate substandard drugs from the American market with as little confusion as possible, so that physicians can rely upon the accuracy of the remedial agents which they prescribe or dispense.

"To this end the continued co-operation of the industry is invited. There can be no doubt of the possibility of mutual helpfulness, and indeed, of general benefit, from an exchange of information and the results of research on such subjects as the supervision and control of the manufacture of potent drugs."

What is a Potato?—Science often upsets the popular classification of objects. It teaches us that the eel is not a snake, the whale not a fish, the bat not a bird and so on. In the recently published 1925, report of the Smithsonian Institution a reprint is given of a paper by William E. Safford contributed to the Journal of Heredity, (1925, Vol. 16) on "The Romance and Reality of the Potato." It appears that the name properly belongs to the "sweet potato," Ipomoea batatas, a member of the Convolvuaceae, the well-known "morning glory" family. The white potato is commonly called in the United States the "Irish potato." Several plants were confused by the earlier writers on the vegetation of America. It has been supposed that the white potato was taken from North America to Ireland, but the reverse is the case. A Virginia plant stated to have figured in this emigration, is a member of the bean family. The name Solanum tuberosum was given first to the plant producing the white potato by Kaspar Bauhin in 1596, and subsequently adopted by Linnaeus. It was introduced into Europe from Peru probably by Spaniards. It was more than a century before its great food value was fully recognized. It was in Ireland that the most active cultivation started. The climate and soil are there very favorable to it. The exact date of the beginning of active cultivation is unknown but existing records show that in 1663 the Royal Society was advised of its value as a food crop. Irish peasants devised many methods of preparing the tuber and also discovered its value as a source of strong spirit.

In 1719 some Scotch-Irish emigrants established a settlement in New Hampshire, which they called Londonderry, and brought with them the potato. Their first crops were potatoes and flax. This was the beginning of the extensive cultivation of the plant in America. At first, colonists other than the Scotch-Irish were so unfamiliar with the plant that they tried to use the fruit and found it unpalat-

able. The following year, in ploughing the ground, many fine tubers were turned out and thus the true yield of the plant was indicated.

The wild form of  $Solanum\ tuberosum\ L$ , has never been found. The cultivation in South America dates long before the Columbian era, but never spread as far north as the shore of the Caribbean Sea. The "potato" reported by earlier navigators and visitors to that region is the "sweet potato." Evidences of early culture of the white potato are curiously proved by pottery found in prehistoric tombs in certain parts of South America as well as by numerous dried specimens of the tubers themselves.

The cultivation of the potato in Germany gave rise to its extensive use as a source of alcohol and from this "potato spirit" was obtained a considerable portion of the higher alcohols, collectively known as fusil oil, of which the principal ingredients—pentyl alcohols—derive their common name "amyl" from the Greek for "starch."

The paper is illustrated by photographs of plants that have been confused with the true white potato, pictures of prehistoric pottery showing conventionalized tubers and other data of interest. Safford shows that the stories ascribing to Sir Walter Raleigh and to Sir Francis Drake the introduction of the potato into England are without foundation of fact.

HENRY LEFFMANN.

# NEWS ITEMS AND PERSONAL NOTES

UNITED STATES CIVIL SERVICE EXAMINATION

The United States Civil Service Commission announces the following open competitive examination:

# JUNIOR PHARMACIST

Aplications for junior pharmacist must be on file at Washington, D. C., not later than February 12. The date for assembling of competitors will be stated on their admission cards and will be about ten days after the close of receipt of applications.

The examination is to fill vacancies in the Public Health Service throughout the United States, and in positions requiring similar qualifications.

The entrance salary is \$2,500 a year. After three years of satisfactory service and the passing of a satisfactory physical and professional examination promotion is made to the grade of pharmacist at \$3,000 a year, and further promotion is made to the grade of chief pharmacist at \$3,500 a year after ten years of service from date of original appointment as junior pharmacist and the passing of a satisfactory physical and professional examination.

The duties will include the purchasing, selecting, and compounding of drugs and medicinal agents to be used at the hospitals and relief stations of the Public Health Service; the handling of correspondence, requisitions and bids for supplies and the supervision of subordinate personnel. The duties of chief clerk, registrar, material officer, and other such duties may be assigned by the officer in charge at hospitals or relief stations, quarantine, immigration investigation and epidemic control stations of the Public Health Service.

Competitors will be rated on spelling; pharmaceutical and chemical arithmetic; essay or report writing; chemistry, pharmacy, and materia medica; and their education, training, and experience.

Full information and application blanks may be obtained from the United States Civil Service Commission, Washington, D. C., or the secretary of the board of United States Civil Service Examiners at the post office or custom house in any city.

AMERICAN PHARMACEUTICAL ASSOCIATION ELECTS OFFICERS.—The result of the election of the American Pharmaceutical Association has just been announced by the Board of Canvassers who are William B. Day, William Gray and Charles H. Avery, of Chicago.

The results are:

President, Charles W. Johnson, State of Washington; First Vice-President, Ambrose Hunsberger, of Pennsylvania; Second Vice-President, Joseph Jacobs, of Georgia; Members of the Council, H. V. Arny, of New York; Theodore J. Bradley, of Massachusetts, and George M. Beringer, of New Jersey.

PHILADELPHIA BRANCH ENDORSES WASHINGTON.—The Philadelphia Branch of the American Pharmaceutical Association at its regular January meeting unanimously passed a resolution giving entire support of the Branch to Washington, as the proper and logical site for the headquarters building.

Philadelphians, of course, had the interest of their own city at heart and there are many reasons why Philadelphia would be a very suitable place for the headquarters building. It is one of the largest pharmaceutical centers of the country. The A. Ph. A. was founded in Philadelphia and it is a national historic shrine. However, the members of the Branch felt that even their loyalty for Philadelphia should be set aside for the good of the Association and Pharmacy as a whole, as they felt that Washington was the logical and proper place for the building. The future of Pharmacy depends greatly on legislation and Washington is the natural center for this work. It is also the shrine of the nation—the most beautiful city of the country and a place where the headquarters building would stand amid ideal surroundings as a national memorial to Pharmacy.

The Branch, therefore, gives its entire support to Washington and urges that other members of the American Pharmaceutical Association consider Washington as first choice for the headquarters building.

ADLEY B. NICHOLS, Secretary.

THE THIRTY-SECOND CHEMISTS' EXHIBITION, organized by the "British and Colonial Pharmacist," will be held in the Holland Park Hall, London, W., from May 9-13, 1927. All members of the drug and chemical trades who are in England during the week, will receive a cordial welcome on presentation of their professional or business cards. The exhibition will be the largest yet held and will contain much of interest to all connected with pharmacy and allied callings.

# **BOOK REVIEWS**

Annual Reports of the American Medical Association Chemical Laboratory. 199 pages, illustrated. Press of the American Medical Association, Dearborn Street, Chicago. Paper \$1.25.

A fearless compilation of reports from the chemical laboratories. of the American Medical Association, explained and elaborated in the literary laboratory of the same institution, comprises this little volume. Another organization would hardly have had the courage, and the resources, to continue anually with this work.

This particular phase of the activities of the American Medical Association might well have been undertaken from the outset by organized pharmacy, yet it is quite conceivable that certain accomplishments now recorded could never have come to pass under Pharmacy's overseership.

Many of the extra-pharmaceutical evils, the subduance of which was made possible by the well-organized work of the A. M. A. would still be extant had they not been attacked by a power outside of pharmacy.

The vicious dope-containing nostrum—the pseudo-synthetic—the arrant cancer quackery, and its kind are, thanks to this work, banished forever.

In the standardization and control of new and unofficial remedies done under the direction of the Council, and records of part of which work appear in this little volume, a great deal of real good has been accomplished.

The analytical methods utilized by the Association's laboratory are appended and may prove their usefulness to others pursuing a like investigation.

Certainly the little volume is well worthy of inclusion in the practicing pharmacist's library.

IVOR GRIFFITH.

ILLUSTRIERTER APOTHEKER-KALENDER, 1927. Bearbeitet von Apotheker Fritz Ferchl, Mittenwald. Mk. 4.50. Deutscher Apotheker-Verein, Levitzowstr. 16B, Berlin, N. W. 87.

The zealous pharmaceutical historian and manager of the Marien-Apotheke in Mittenwald (Bavarian Highlands) and treas-

urer of the newly formed Society for History of Pharmacy, herewith presents the third edition of his excellent Illustrated Pharmacist's Calendar. It is arranged in pages which can be separated or turned over, containing from two to four dates at the bottom, the upper part being used for the illustrations together with explanations. The referee herewith classifies the latter into the following groups:

- I. Photos with biographical notes. These range from Cosmas and Damian, the patron saints of Pharmacy, the Arabian physician Avicenna (980-1037), the Dutch chemist, J. B. van Helmont (1577-1644), the discoverer of CO<sub>2</sub> and H<sub>2</sub>S, the much abused physician, teacher and philosopher Philippus Aureolus, Theophrastus, Bombastus von Hohenheim, better known as Paracelsus (1493-1541), iconoclast of medicine and father of iatro-chemistry, the apothecary Johann Friedrich Boettger (1685-1719), the inventor of German porcelain, the French pharmacist Antoine Baumé (1728-1804), whose hydrometer scale is still in use today, up to Apotheker Dr. Heinrich Salzmann of Berlin, who on August 29, 1927, will celebrate the twenty-fifth anniversary as president of the Deutscher Apotheker Verein.
- 2. Title Pages of Pharmacopæias, as f. i. Augustana, 1564, Colonensis 1628, Antwerp edition of Valerius Cordus 1652, etc.
- 3. Drug Pots made of Wood, Glass, Clay, Majolica, Fayence and Porcelain.
  - 4. Apparatus, Alchemistic and Pharmaceutical.
  - 5. Mortars. Among these is one dating back to 1400.
- 6. Apothecary Shops and Buildings. From an old Chinese drug store, the Winkler Apotheke in Innsbruck originated in the thirteenth century, the Rats-Apotheke in Goslar 1301, the Hirsch-Apotheke in Halle 1535, the Kugel-Apotheke in Nuernberg 1654, to Scheele's Apothecary Shop in Köping, Sweden, about 1775. These photos cover historical buildings in many countries.

The Illustrierter Apotheker-Kalender is just the thing to ornament the pharmacist's library, prescription department or laboratory. It will awaken in him and the younger generation a love for their profession. The author, Fritz Ferchl, and the publisher, the Deutschen Apotheker-Verein deserve the thanks of the entire pharmaceutical profession for this work of art.

Otto Raubenheimer, Ph. M.

LE MONDE VEGETAL CHEZ LES HEBREUX. USAGES ET COUTUMES. Par A. Nickles, Pharmacien de re Classe. 114 pp. Imprimiere Jobard, Dijon. 10 frs.

This historical monograph written by a pharmacist in Besancon, is another vivid illustration of the increase in the knowledge of the history of pharmacy. The introduction is by Ph. Eberhardt, Professor at the Faculty of Sciences in Besancon. Pharmacien Nickles has divided the subject as follows: Geography, Climate, the Hebrews and their Neighbors, and the Vegetable Materia Medica. The latter is arranged in alphabetical order from "Apricot" to "Wine." Copious foot-notes, a bibliographic index, and an excellent subject index are distinct advantages. I might also mention that the monograph is sold for the benefit of the blind of the war, certainly a worthy cause.

OTTO RAUBENHEIMER, Ph. M.

Pharmacy in Europe.—The January number of the *Drug Edition* of the *New York American Merchandiser* contains an article on this subject, based on an interview with Prof. Otto Raubenheimer, a well known Brooklyn pharmacist and member of the N. F. Revision Committee, who made a four-months' tour through different ports of Germany, Austria, Northern Italy, Switzerland, the Saar District (now occupied by the French) and Holland, and made a close study of conditions in pharmacy and chemistry. The paper is divided into the following chapters: Pharmacies, Government Control, Drug Stores, Colleges, Women in Pharmacy, Working Hours, Standard Prices, Conditions in Pharmacy and Society for History of Pharmacy.

In most Continental Europe, pharmacies are under strict governmental control and are restricted as to number, *i. e.*, an apothecary shop to about 6,000 inhabitants. In order to open a new pharmacy the apotheker must first obtain a concession from the authorities. The following requirements are taken into consideration: Need and location of the new pharmacy and age, nationality, fitness and financial standing of the applicant. Needless to say, there is always a long waiting list and an apotheker usually attains the ripe age of fifty before he obtains a concession to open a new apothecary shop. Apothecaries are obliged to charge according to a tariff scale which is issued and revised by the government. To the fixed price for each

and every ingredient there is added a charge for the container and, last but not least, in fact most important, "for knowing how to compound the prescription," a charge which is frequently neglected by the American pharmacist.

Drug stores are quite numerous, but are not allowed to sell poisonous articles nor compound prescriptions. In two instances, both in Bavaria, and both in summer resorts, Dr. Raubenheimer found a pharmacy and drug store combined under the same ownership. Special government permission has to be obtained for such a combination.

The educational requirements of an Apotheker are as follows: High school graduation, two years' apprenticeship, assistant examination, one year practical assistantship, four semeters of university, pharmacist's examination (written, oral and practical), two years of practice as provisor and then a full-fledged Apotheker. It can thus be seen that a total of at least seven years of practical and university training is required. No wonder pharmacy is on a higher scale in Germany than elsewhere.

The paper concludes with a note on the newly formed Society for History of Pharmacy which has the object to acquaint the pharmacist with the history of his profession, thus gaining him access by giving him a more cultured background and maintaining the impression among his customers and the medical profession that he is a man of education and culture. More particulars about this new Society can be found on pages 680 and 681 of the December number of the American Journal of Pharmacy.